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RESEARCH ARTICLE

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Abstract In the cat it is known that the distribution and modulation of the so-called P2 responses are similar, irrespective of whether they are obtained with electrodes implanted in the different skin areas or in the various leg muscles. In man it is known that the specific stimulation of cutaneous afferents from different parts of the foot evokes P2 responses, the phase-dependent modulation pattern of which exhibits both location-specific and common features. Responses generally differ, but one striking feature is the occurrence of suppressive responses in the tibialis anterior (TA) of the ipsilateral (i) leg at the end of the swing phase independent of the nerve stimulated. The question arises of whether this aspecificity is limited to the foot. Can similar suppressive P2 responses in iTA be obtained when afferents outside the region of the foot are stimulated during walking? If so this would indicate that there is a very general suppression occurring of input to the TA motor neuron pool, for example through presynaptic inhibition of a corticospinal drive. To answer this type of question the motor responses following transcutaneous stimulation of the rectus femoris (RF) and the motor responses following stimulation of the femoral nerve branch innervating the skin area above the quadriceps were determined during human locomotion. Electromyographic (EMG) activity in iTA was recorded by means of surface electrodes. In all subjects (N=10), the first consistent responses following RF stimulation occurred at about 80 ms poststimulus. The amplitude of these responses showed a clear phase-dependent modulation pattern. Facilitatory responses occurred during the end stance and early swing phase and turned into suppressive responses at the end of the swing phase. To investigate whether cutaneous afferents overlying the RF determined some of the responses following transcutaneous RF stimulation, the experiments were repeated following local anesthesia of the skin under the stimulation electrodes. This did not affect the responses substantially, indicating that most of the RF stimulation results were related to activation of muscle afferents. A similar phase-dependent modulation pattern was found following stimulation of cutaneous afferents of the femoral nerve (Fn). However, this phase-dependent modulation pattern was less pronounced and less consistent over the subjects when compared to the one found following RF stimulation. Our first conclusion is that the results show that P2 reflexes can be elicited both by stimulation of cutaneous afferents in the foot and by proximal cutaneous nerve and muscle stimulation. Secondly, it can be concluded that the suppressive responses at the end of the swing phase are present for both RF stimulation and stimulation of cutaneous afferents of the foot. This result indicates that a wide variety of afferent inputs have a suppressive influence on the input drive to TA motor neurons just prior to heel strike.

Keywords Tibialis anterior · Cutaneous nerve stimulation · Muscle stimulation · Phase-dependent modulation · EMG · Human walking

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Introduction

It is well known that the way in which specific afferent input changes the motor output during locomotion is

dependent on the phase in the step cycle. This was extensively studied for human walking when cutaneous afferents in the foot were stimulated (Duysens et al. 1990; Tax et al. 1995; Van Wezel et al. 1997; Yang and Stein 1990; Zehr et al. 1997). Electrical stimulation of cutaneous nerves in the foot elicited responses of about 70–80 ms poststimulus in both ipsi- and contralateral leg, and the amplitude of these responses was dependent on the phase of stimulation (Van Wezel et al. 1997; Zehr et al. 1997). The amplitude of these so-called P2 or middle latency (ML) responses could even change from facilitatory into suppressive responses within the step cycle (Duysens et al. 1990; Tax et al. 1995; Van Wezel et al. 1997; Yang and Stein 1990; Zehr et al. 1997). Furthermore, it was shown that stimulation of different cutaneous nerves in the foot (sural, peroneal, and posterior tibial nerves) yielded P2 responses with both nerve-specific and nerve-aspecific features (Van Wezel et al. 1997; Zehr et al. 1997). Facilitatory P2 responses were present in the ipsilateral (i) tibialis anterior (TA) at the end of the stance phase when the sural nerve was stimulated, but not, or very seldom, when the other cutaneous nerves (peroneal and posterior tibial nerves) were stimulated (Van Wezel et al. 1997; Yang and Stein 1990; Zehr et al. 1997). In contrast, suppressive P2 responses occurred in the iTA at the end of the swing phase independent of the nerve stimulated. The occurrence of common suppressive reflex action independent of the nerve stimulated can be explained if the excitatory drive to TA is somehow blocked following various sensory inputs, perhaps to prevent inadvertent TA activation in this critical touch-down period. Because of this remarkable finding, the question arose of whether this suppression is even more generalized and not limited to the nerves innervating the foot only. Such generalized effects would not be totally unexpected in the light of previous work on animals. In cats it was found that stimulation of various muscles or different sites of the skin in upper and lower leg yielded similar P2 reflexes (Abraham et al. 1985; Duysens and Loeb 1980: for review, see Rossignol et al. 1988).

In the present study we investigated whether such generalized reflex effects also exist in humans by examining the iTA motor responses following electrical stimulation of afferent sites other than the earlier described cutaneous nerves of the foot. For this purpose, the motor responses in iTA following an electrical evoked contraction of an upper leg muscle (rectus femoris) were studied in the first part of the experiment. Such stimuli activate both muscle and skin afferents. A contraction of the rectus femoris (RF) was achieved through transcutaneous electrical stimulation and not through implanted wires (as was done by Duysens and Loeb 1980 in cats). Although we specifically wanted to stimulate the RF, the method of transcutaneous stimulation cannot avoid that cutaneous afferents under the electrodes are stimulated too. To check to what extent the responses to RF stimulation might be due to stimulation of the skin under the electrodes, the RF stimulation experiment was repeated in a different set of experiments with local anesthesia of the skin under the stimulation electrodes.

In the second part of the experiment the motor responses in iTA following stimulation of the nerve innervating the skin area above the quadriceps (sensory part of the femoral nerve) were determined.

Preliminary results have been published in abstract form (Van de Crommert et al. 1998).

Materials and methods

Experimental setup

The data presented in this article were collected during two separate experimental sessions. The first session consisted of electrical stimulation of the rectus femoris (RF) and the femoral nerve (Fn). Ten subjects participated in the RF stimulation experiment and eight out of these ten subjects participated in the Fn stimulation experiment. A different group of nine subjects took part in the second session of the experiment during which the RF was stimulated with and without local anesthesia under the stimulation electrodes. The subjects were aged between 23 and 31 years and had no known history of neurological or motor disorder. The subjects' task was to walk at a constant pace on a treadmill with the belt-speed set at 4 km/h. The tests were performed in conformity with the principles described in the Declaration of Helsinki for experiments on humans.

For stimulation of the RF two self-adhesive stimulation electrodes (Biomedical Life Systems: Bioderm skin mounts: 4.3×4 cm) were positioned longitudinally over the muscle (inter-electrode distance of approximately 15 cm) of the left leg. This was done in such a way that the stimulus primarily evoked a contraction in the RF. However, because of the size of the electrodes, it was possible that nearby muscles, belonging to the quadriceps, were recruited as well.

The RF was stimulated with six different stimulus intensities which were based on three intensity-related reference points (thresholds). These thresholds were determined during quiet standing. In order of increasing intensity these thresholds were:

1. Perception threshold (PT); stimulus intensity which can just be sensed by the subject
2. Muscle contraction threshold; stimulus intensity for which the stimulated muscle makes a just perceivable contraction (determined by the investigator)
3. 'Pain' threshold; intensity that gave an unpleasant sensation to the skin under the electrodes (determined by the subject).

The lowest stimulus intensity was set just above the muscle contraction threshold. The highest intensity was as high as tolerated by the subject but never more than the pain threshold. The other four intensities were linearly interpolated between the lowest (I=1) and highest (I=6) intensity. No stimulus intensity between perception and muscle threshold was applied since preliminary experiments (four subjects were involved) showed that no reflex responses occurred at these intensity levels.

For the RF stimulation experiment with local anesthesia, one intensity (I=5) was applied. First, the RF was stimulated without the anesthetic cream. Afterwards, the stimulation electrodes were removed and 5 g of anesthetic cream [EMLA; Pharmaceutica BV, Zoetermeer, active ingredient lidocaine (25 mg/g) and prilocaine (25 mg/g)] was put on each skin area (surface approximately 5×5 cm) where the stimulation electrodes were previously attached, and covered with special plasters. After a pause of 2 h, the cream was removed and the stimulation electrodes were attached to the skin again and the RF stimulation experiment was repeated. The effect of the EMLA cream on the PT after removing the plasters is

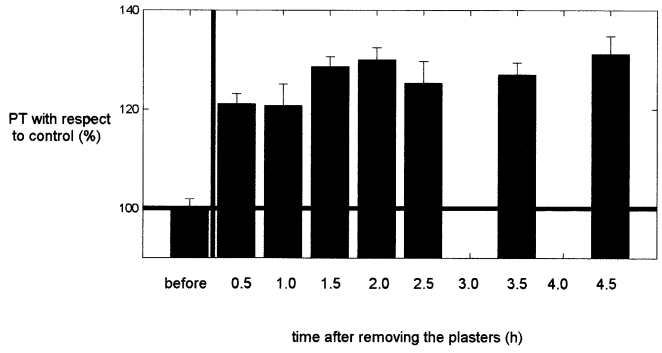

Fig. 1 The change in perception threshold (±SD) after the use of the anesthetic cream (EMLA) as function of time (*h*) after removal of the plasters for one subject. The change in PT following local anesthesia is given with respect to PT of the control (not anesthetized) leg

shown in Fig. 1 for one subject. It can be seen that PT increased by 20–30% relative to the PT as measured for the other leg.

This type of anesthesia is likely to affect mostly superficial layers. In order to determine whether the EMLA cream mainly affected superficial or deep sensations, pencil scratches with different degrees of pressure were applied on the skin during the control and EMLA condition. During the EMLA condition it was clear that the subjects did not sense the pencil scratches with light pressure any longer. With higher pressure the pencil was perceived but the feeling changed (to a "numb" like feeling) as compared to the control condition.

For cutaneous nerve stimulation, an electrode (poles of 0.5 cm in diameter and a fixed interelectrode distance of 2.0 cm) was positioned over the sensory part of the Fn (about 5 cm below the inguinal ligament in the direction of the RF) of the subjects' left leg. The exact location of the stimulation electrode was determined according to the optimal irradiation in the skin overlying the RF and care was taken that no muscle contractions were elicited. The stimulus electrode was kept in position with elastic straps. For stimulation of the Fn, one intensity was applied. The intensity was 6 times PT and the stimuli were not painful according to the subjects.

For both transcutaneous muscle and cutaneous nerve stimulation the electrical stimulus consisted of a train of 6 ms duration during which three bipolar pulses of 2 ms duration were given. A custom-made constant-current amplifier delivered the current intensities chosen.

Activation of TA in the ipsilateral leg was measured by an electromyogram (EMG) recorded by means of surface electrodes. The raw EMG signals were preamplified (10 times) close to the subject to minimize signal distortion. Then, the EMG signals underwent a second amplification (adjustable from 0.25 to 5.0×10^5), high-pass filtering (cut-off frequency at 3 Hz), full-wave rectification, and low-pass filtering (cut-off frequency at 300 Hz), similar to methods as reported in previous publications (Duysens et al. 1996; Van Wezel et al. 1997). A very thin insole switching system was used for the detection of foot contact (designed in collaboration with Algra Fotometaal b.v., Wormerveer, The Netherlands).

Experimental protocol

Before the experiments started the subjects had become accustomed to walking on the treadmill and were able to walk at a constant pace with the belt speed set at 4 km/h. Furthermore, the subjects were familiarized with the electrical stimuli as used during the experiments.

The stimuli were characterized by their time of occurrence during the step cycle and by their intensity. For variations in timing, the step cycle duration (determined during a stable walking pattern prior to the experiment) was divided into 16 equal time-intervals (i.e., phases). Phases one and nine corresponded to left and right heel strike, respectively.

To distinguish EMG responses from normal background EMG activity, trials without stimulus were measured as well. All conditions (determined by phase and by stimulus intensity) occurred ten times in random order with a random interval of 3.5–5 s. This corresponded to at least two cycles of unperturbed walking. Left or right footfall triggered a computer to start a trial with a preprogrammed delay. The specific trial was measured from 100 ms before stimulation until 1500 ms post stimulus. All signals (stimulus' voltage and current, EMGs, and foot contacts) were AD converted at a frequency of 500 Hz and stored on hard disk with a condition-specific code to enable data analysis. Another computer system enabled the online inspection of data.

Data analysis

The first step in data analysis was the construction of the mean of the ten trials for all conditions. This resulted in a set of 'control' (without stimulation) and a set of 'response' data. The net EMG response was obtained by subtracting the control data from the corresponding response data.

The latency or onset of the first consistent responses was about 80 ms poststimulus. The amplitude of these responses was quantified with a single time-window (set by visual inspection of the data) for all phases (and for all intensities for RF stimulation). Within this time interval the mean EMG activity of all original control and response trials (n=10 per condition) was calculated. From these window-averaged trial data, the mean and standard error (SE) of the response amplitudes were obtained. Subsequently, the resulting data were normalized with respect to the maximum control values as seen in the window-averaged control data in order to enable proper intersubject comparison. The statistical significance of the responses was tested with a Wilcoxon matched-pairs signed rank test (p<0.05). The mean EMG amplitudes of the individual trials from control and response data formed the ten matched pairs. A similar test was used to determine whether the responses following RF stimulation without and with local anesthesia under the stimulation electrodes differed significantly.

Results

Electrical stimulation of the rectus femoris

On the basis of the EMG responses in all subjects, we classified the responses following RF stimulation into three groups, namely: early, middle, and late latency responses (EL, ML, and LL responses, respectively). The EL, ML, and LL responses had a latency of about 50, 80, and 105 ms, respectively. Since the latency of the ML responses corresponds with the latency of the earlier described P2 responses following cutaneous nerve stimulation of the foot (see "Introduction"), the ML responses are the main focus of this report and will also be called P2 responses from now on.

Single subject

The first step in data analysis was the determination of the mean of the ten trials for both the control and stimulus data for each phase of the step cycle. An example of such

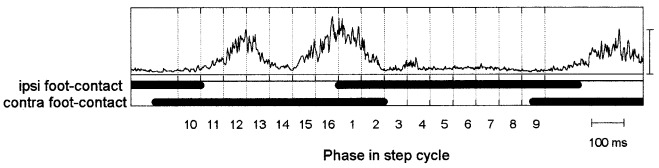

Fig. 2 The mean control EMG activity (n=10) of iTA in subject 1 during one step cycle. Ipsi- and contralateral foot-contact are plotted below the iTA EMG activity. Time calibration: 100 ms; EMG calibration: 1 mV

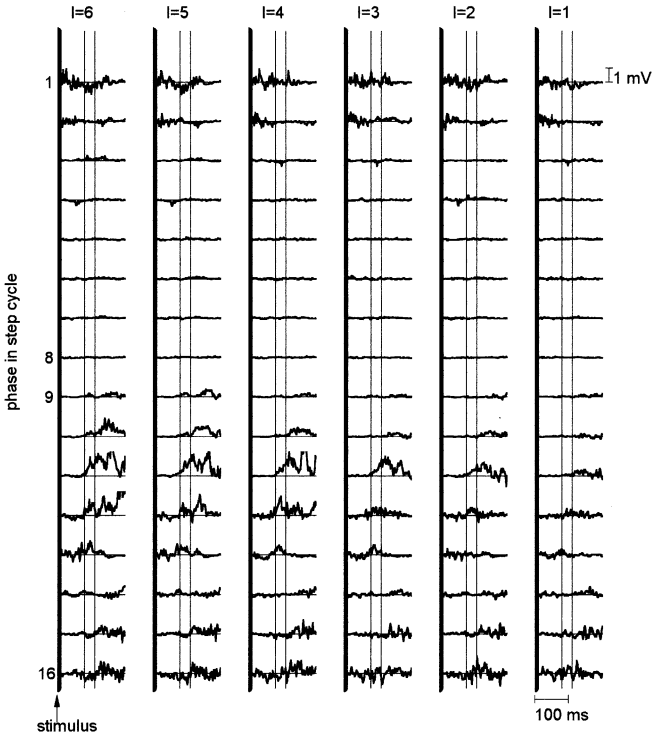

Fig. 3 Subtracted iTA EMG activity of subject 1 for all phases and intensities following RF stimulation. A typical set of 96 average (n=10 trials) subtraction traces is shown (0–200 ms poststimulus). For each intensity (I=6 to I=1), the 16 phases are plotted beneath each other. Phases 1–10 and phases 11–16 correspond to the ipsilateral stance and swing phase, respectively. The *thin solid lines* indicate the time window that was set for the quantification of the P2 responses. Time calibration: 100 ms; EMG calibration: 1 mV

a set of control data and the division of the step cycle into the subsequent phases can be found in Fig. 2.

The reflex effect of stimulation was obtained by subtracting the control data from the corresponding (i.e., similar phase and stimulus intensity) response data. Hence, this resulted in 96 traces with subtracted data (16 phases and 6 stimulus intensities) for each subject. Figure 3 shows such a set of subtracted traces of iTA (0–200 ms poststimulus) for subject 1. For each intensity, the responses for the 16 different phases are plotted beneath each other.

The first consistent responses appeared at about 80 ms poststimulus (P2 response). At phase 1, the P2 response is

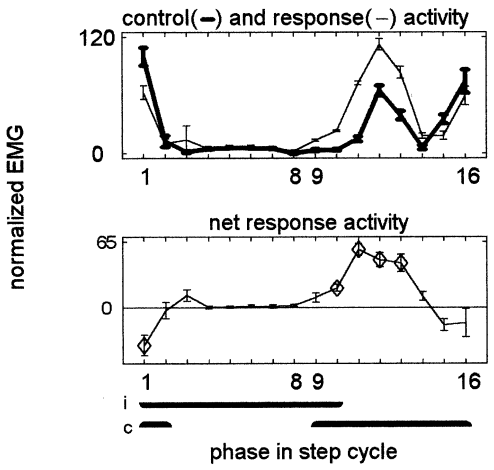

Fig. 4 The quantitative representation of the P2 responses in iTA of subject 1 following stimulation of the RF with the highest intensity (I=6). At the *top of the figure*, both control and response activity (±SE, n=10 trials) are shown. At the *bottom of the figure*, the resulting subtracted data (±SE) are shown. The statistical significance of the responses (p<0.05) is indicated by *diamonds*. The data are normalized with respect to the maximum locomotor activity (100) as seen without stimulation. The ipsi- and contralateral stance phases are plotted below the subtracted data

suppressive (i.e., less than control EMG activity). No responses occurred at phases 2 until 8. For phases 9, 10, and 12, two separated facilitatory (i.e., more than control EMG activity) responses (P2 and LL response) can be distinguished. At phase 11, a response with latency of 80 ms and long duration was elicited. At phase 13, only a P2 response was elicited. At phase 15 and 16 the P2 responses were mostly suppressive and were followed by facilitatory LL responses. When we compare the responses following stimulation at the different intensities, it can be seen that the responses diminish gradually (decrease in amplitude and duration) when stimulus intensity decreases from I=6 (highest) to I=1 (lowest). On the basis of these subtracted traces, the window for quantification of the P2 responses was set at 80–105 ms poststimulus as indicated with two thin lines (the beginning and end of this window were mainly based on the phases when P2 responses were detectable as separate responses: phases 1, 9, 10, 12, 13, 15, and 16). Within this window the mean of the control and response trials (n=10) were calculated and subjected to a Wilcoxon test (see "Materials and methods").

In Fig. 4, the quantified P2 responses in iTA following stimulation at the highest intensity for subject 1 are presented. At the top of the figure, both control and response activity are shown. The resulting subtraction data with corresponding significance can be found at the bottom of the figure. As can be seen, there were no P2 responses during most of the stance phase (phases 2–8). From end stance to early swing (phases 9–13), statistically significant (indicated with diamonds) facilitatory P2 responses with increasing amplitude occurred. At the second half of the swing phase and the beginning of the

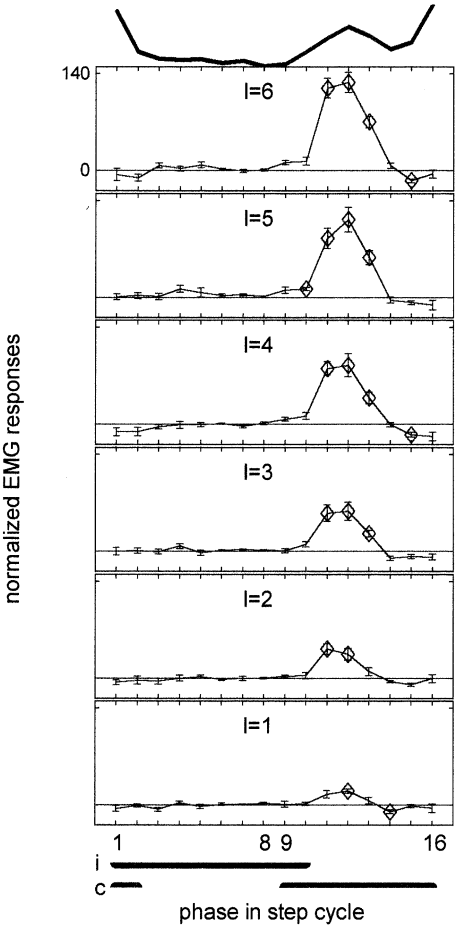

Fig. 5 Population average (N=10 subjects) of the subtracted P2 responses (±SE) in the iTA following stimulation of the RF of all applied intensities (I=6 to I=1). The statistical significance of the responses (p<0.05) is indicated by *diamonds*. At the *top of these figures* the background activity of the iTA is shown. The data are normalized with respect to the maximum locomotor activity (100) as seen without stimulation. The ipsi- and contralateral stance phase are plotted at the *bottom of the figure*

stance phase (phases 15, 16, and 1), these facilitatory responses turn into suppressive ones (significant at phase 1).

Population average of P2 responses

The same procedure as described above was carried out for all subjects. The mean latency of the P2 responses following RF stimulation was 81±5 ms and they had a mean duration of 26±5 ms. The population averages of the subtracted P2 responses following stimulation with the six different intensities are given in Fig. 5. At the top of the figure, the background activity of the iTA is shown as well.

In iTA, no responses occurred during the stance phase, while from early to mid swing phase large facilitatory responses were elicited. The facilitatory responses turned into suppressive ones at the end of the swing phase. An

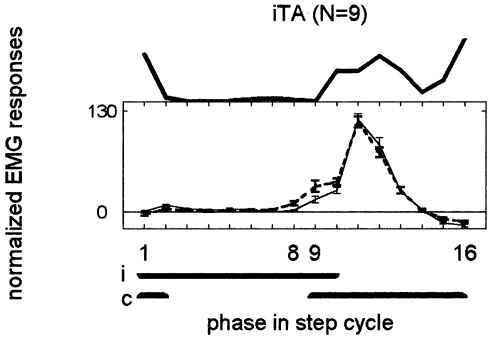

Fig. 6 Population average of the subtracted P2 responses (±SE) in the iTA following stimulation of the RF without (*solid line*) and with (*dashed line*) local anesthesia of the skin under the electrodes. A similar format is used as for Fig. 5

increase in intensity of the stimulus yielded mainly an increase in the amplitude of the facilitatory responses while there was little effect on the amplitude of the suppressive responses. However, the basic phase-dependent modulation pattern of the P2 responses in the iTA was unchanged when different stimulus intensities were compared (see Fig. 5).

Electrical stimulation of the rectus femoris with local anesthesia

The phase-dependent modulation of P2 responses in the iTA following RF stimulation without and with local anesthesia of the skin under the electrodes was studied in a separate group (see Fig. 6). The results without anesthesia agree with those observed in the previous group. Furthermore, it can be seen that the basic features of the phase-dependent modulation pattern were preserved when the skin under the electrodes was anesthetized. None of the EMG responses differed significantly (p<0.05) from each other for the two conditions.

Electrical stimulation of the femoral nerve

Electrical stimulation of the Fn elicited responses with latency of 81±5 ms and duration of 24±5 ms. Since latency and duration coincide with the latency and duration of the responses following RF stimulation (81±4 ms and 26±5 ms, respectively), these responses will be called P2 responses too. The quantitative representation of the P2 responses as the mean of the whole population (N=8) is found in Fig. 7.

The amplitude of the facilitatory P2 responses elicited by Fn stimulation was much smaller than the amplitude of the RF-induced P2 responses following stimulation with the highest intensity. The mean phase-dependent modulation pattern of the Fn stimulation induced responses in iTA was about similar to the one obtained following RF stimulation with the lowest intensity: small facilitatory P2

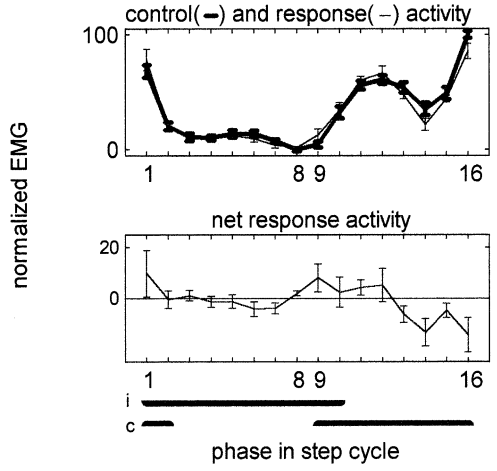

Fig. 7 Population average (N=8 subjects) of the subtracted P2 responses (±SE) in the iTA following stimulation of the Fn. A similar format is used as for Fig. 4

responses at the transition from stance into swing and suppressive P2 responses at the end of the swing phase. In contrast to the responses obtained following RF stimulation, the responses following Fn stimulation were not significant over the different subjects.

Discussion

The main finding of the present paper is that P2 (or ML responses) are not restricted to stimuli given to the foot but are also present for stimulation of afferent volleys in the upper leg. Furthermore, the phase-dependent modulation pattern of these responses bears some similarity to those found following stimulation of cutaneous nerves of the foot.

P2 responses following RF and Fn stimulation

Both RF and Fn stimulation during gait yielded P2 responses with a latency of about 80 ms and a duration of about 25 ms in iTA. The amplitude of the P2 responses following RF stimulation showed a clear dependency on the phase in the step cycle. The phase-dependent modulation pattern of these responses was dependent on the intensity stimulated (see Fig. 5). An increase in stimulus intensity yielded mainly an increase in the amplitude of the facilitatory responses while there was little effect on the amplitude of the suppressive responses. Secondly, it can be seen that the number of significant responses decreased with decreasing stimulus intensity, i.e., the responses became less expressive over the subjects. For this reason, the present report mostly focused on the phase-dependent modulation pattern following stimulation at high intensities (i.e., I=3 to I=6). The main phase-dependent modulation pattern in TA consisted of facilitatory P2 responses from end stance until mid swing phase and suppressive responses at the end of the swing phase. The facilitatory responses at the transition from stance into swing phase were consistent over the different stimulus intensities. Instead, the small suppressive responses at the end of the swing phase were significant only for stimulus intensity 4 and 6. Although not significant at intensities 3 and 5, suppressive responses were still present for eight out of the ten subjects investigated.

The phase-dependent modulation of the P2 responses was basically the same for both RF and Fn stimulation but the amplitude of the facilitatory P2 responses following Fn stimulation was much smaller than the responses following RF stimulation with the highest intensity. The amplitude of the P2 responses following Fn stimulation resembled most closely the amplitude of the P2 responses following RF stimulation with the lowest intensity. Furthermore, the responses following Fn stimulation were more variable than the responses obtained following RF stimulation (i.e., no significant mean responses occurred as seen over the whole population). Nevertheless, five out of eight subjects showed facilitatory responses at the transition from stance into swing phase and six out of eight subject showed suppressive responses at the end of the swing phase.

Since the Fn innervates the part of the skin overlying the quadriceps, the tendency towards a similar modulation pattern for RF and Fn stimulation could indicate that the P2 responses following RF stimulation were mainly caused by the local activation of the cutaneous afferents under the stimulus electrodes.

To evaluate the above-mentioned possibility, an additional experiment was performed. The RF stimulation experiment was repeated with local anesthesia of the skin under the electrodes. In this way, we can assume that electrical activation of the cutaneous afferents under the electrodes is reduced (see “Materials and methods”). The reduced cutaneous afferent input did not affect the responses substantially. This indicates that the cutaneous afferents under the stimulation electrodes had a minimal contribution to the observed P2 responses following RF stimulation.

This result may seem in contradiction to the results obtained following Fn stimulation since similarities between the P2 responses following Fn and RF stimulation do exist. However, one should take into account that Fn was likely to activate nerve afferents much more effectively than transcutaneous muscle stimulation. From experiments in which cutaneous afferents of the foot were stimulated, with the same method as for Fn stimulation, it is known that clear reflex responses with large amplitudes were readily evoked at low intensities (usually 2 times perception threshold; see Duysens et al. 1990; Tax et al. 1995; Van Wezel et al. 1997; Yang and Stein 1990; Zehr et al. 1997). Hence, the small amplitudes of the P2 responses following strong Fn stimulation (6 times PT) suggests that stimulation of cutaneous afferents of skin overlying the quadriceps is distinctly less effective than stimulation of cutaneous afferents from the foot. This

suggestion is supported by the results of preliminary Fn stimulation experiments on three subjects that revealed no responses when stimulation intensity was below 4 times PT. Furthermore, the finding of responses with small amplitudes when proximal skin sites are stimulated is entirely consistent with results that have been obtained in cats. Duysens and Loeb (1980) showed that stimulation through implanted electrodes in the plantar or dorsal surface of the foot or the lateral surface of the ankle easily evoked responses. In contrast, stimulation through implanted electrodes in proximal skin sites such as the ventral or dorsal surfaces of the knee was much less effective in producing such responses.

Hence, similar to these cat results the most likely interpretation of our Fn data is that stimulation of proximal skin sites is less effective in evoking clear P2 responses as is the case when cutaneous nerves of the foot are stimulated. In addition, this interpretation fits well with the conclusion that the cutaneous afferents under the stimulation electrodes had a minimal contribution to the observed P2 responses following RF stimulation.

The P2 responses following stimulation of the RF versus stimulation of cutaneous afferents of the foot

Transcutaneous stimulation of the RF elicited responses with three different latencies: EL (latency about 50–55 ms), P2 or ML (latency about 80 ms) and LL (latency about 105 ms) responses. The finding of responses with three different latencies is also reported in other studies in which cutaneous nerves of the foot were electrically stimulated during human walking (Annis et al. 1992; Burke et al. 1992; Duysens et al. 1990; Duysens et al. 1992; Tax et al. 1995; Van Wezel et al. 1997; Yang and Stein 1990; Zehr et al. 1997). These responses were classified into three groups: EL or P1 (latency about 50 ms), ML or P2 (latency about 80 ms) and LL or P3 (latency >100 ms) responses. Similar to our P2 responses, the P2 responses following stimulation of cutaneous nerves of the foot were the first consistent responses. The present observation that muscle stimulation elicits similar responses to those seen after skin stimulation is in line with cat data. Duysens and Loeb (1980) showed that the same type of responses (P1, P2, P3), as observed with skin stimulation, were obtained when various leg muscles (such as flexor digitorum longus, FDL and medial gastrocnemius, MG) were stimulated with implanted electrodes. Similarities also extend to the phase-dependent modulation.

The phase-dependent modulation of the presently described P2 responses in the iTA showed most similarities with the results following stimulation of the sural nerve. Both facilitatory responses, at the transition from stance into swing, and suppressive responses, at the end of swing phase, were present. For the other two nerves to the foot (tibial and peronal nerve), the facilitatory responses at the transition from stance into swing phase were not clearly present. In contrast, the suppressive P2 responses were present at the end of the swing phase for both nerves. The common presence of suppressive responses at the end of the swing phase following stimulation of the RF, and all cutaneous nerves of the foot, indicates that these suppressions are not strictly related to the cutaneous afferents in part of the foot only (Duysens et al. 1990; Yang and Stein 1990). The presence of suppressive P2 responses in iTA at the end of the swing phase following stimulation of afferent sites in the upper and lower leg during human walking may point to a common mechanism for controlling these reflexes during rhythmic locomotor movements.

Possible common mechanism involved in the modulation of P2 responses

Such a mechanism for the control of the response amplitude could be of peripheral (interaction between afferents, for example at presynaptic level) and/or of central origin (locomotor circuitry, see Duysens et al. 2000). Several studies (Brooke et al. 1999; Zehr et al. 2001; Duysens et al. 1996) have provided support in favor of the central instead of the peripheral regulation of cutaneous responses of the foot. For example, Brooke et al. (1999) showed that the amplitude of the cutaneous responses was little modulated during passive cycling movement of the leg, indicating that movement-related sensory information did not play an important role in the modulation of cutaneous reflex pathways during cyclic leg movements. In the context of this paper, the present results must then be interpreted as if a central mechanism (at spinal cord, brainstem, and/or supraspinal level) exerts a general suppression during the end of the swing phase on the pathways involved. Recent studies using magnetic stimulation of the motor cortex have shown that TA is easily recruited during the step cycle (Schubert et al. 1997; Capaday et al. 1999; Pijnappels et al. 1998). The cortical induced TA facilitation reached maximal values in TA prior to and during late swing phase. If we assume that the TA burst at end swing is largely due to corticospinal input, then the present data would fit the idea that there is a strong generalized suppression possible of this corticospinal pathway. This suggestion seems plausible since the experiments of Pijnappels et al. (1998) showed that the suppressive responses at the end of the swing phase following sural nerve stimulation were slightly reduced when extra corticospinal input was given.

Functional implications

The suppressive responses in iTA at the end of the swing phase following stimulation of cutaneous nerves in the foot have been described as the proper response to disturbances for the preservation of balance during the step cycle (Zehr and Stein 1999). The suppressive response would lead towards a plantarflexion of the ankle

(Duysens et al. 1992), which at most provides a faster contact of the whole foot on the ground. Our results show that these suppressive responses are not restricted to cutaneous afferents in the foot but have a more general occurrence. This indicates that it must be important for the central nervous system to prevent the activation of ankle dorsiflexors for any of a broad range of perturbations occurring at end swing.

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